

**Notice of Allowability**

Application No.

10/500,319

Applicant(s)

TSUKAMOTO ET AL.

Examiner

Nyeemah Grazier

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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 11/22/04.
2. ☒ The allowed claim(s) is/are 1-5 and 45-49 [now renumbered as claims 1-10].
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of the:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |   |
|---|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)                       |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____. |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),<br>Paper No./Mail Date <u>6/28/04, 10/15/04</u> | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment                               |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material  | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance              |
|   | 9. <input type="checkbox"/> Other _____.  |

**DETAILED ACTION**  
**NOTICE OF ALLOWANCE**

**I. ACTION SUMMARY**

Claims 1-46 are currently pending. Claims 47, 48 and 49 have been added. Claims 6-44 have been canceled by examiner's amendment. The allowable claims are claims 1-5, 45-49.

**II. INFORMATION DISCLOSURE STATEMENT**

The supplemental information disclosure statements filed on June 28, 2004 and October 15, 2004 have been fully considered by the Examiner.

**III. PRIORITY**

This application is a 371 of PCT/US02/37617, filed on December 19, 2002. Applicant claims priority under 35 U.S.C. § 119(e)(1) to U.S. Provisional Application Serial No. 60/342,764 filed on December 28, 2001.

**IV. RESTRICTION-LACK OF UNITY OF INVENTION**

Restriction is required under 35 U.S.C. 121 and 372 because the instant application contains the following inventions or groups of inventions which are not so linked to form a single general inventive concept under PCT Rule 13.1. Therefore a restriction is required according to the provision of PCT Rule 13.2.

The instant application contains Markush practice. However, pursuant to Section B (Markush Practice) MPEP § 1850 (B), the invention does not meet the unity of invention criteria

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because (1) the core structure is not the unifying criteria and (2) the variables do not belong to a “recognized class of chemical compounds in the art to which the invention pertains.” MPEP § 1850 (B) (2004).

Formula (I) as recited in Claim 1 is drawn to an indole compound. The special technical feature is the 1H-indole-2-carboxylic acid. Unity of invention is lacking because the core is not novel, *infra*. Claims 1-46 are drawn to more than one inventive concept (as defined by PCT Rule 13), and accordingly, a restriction is required according to the provision of PCT Rule 13.2.

PCT Rule 13.2 states that the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (requirement of unity of invention). PCT Rule 13.2 states unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.

Annex B, Part 1 (b), provides that “special technical features” mean those technical features, which, as a whole, define a contribution over the prior art.

Annex B, Part 1 (e), provides combinations of different categories of claims and states:

“The method for determining unity of invention under Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:

(i) in addition to an independent claim for a given product, an independent claims for a process specially adapted for the manufacture of the said product, and an independent claim for use of the said product, or

(ii) in addition to an independent claim for a given process, an independent claim for an apparatus or means specially designed for carrying out the said process, or

(iii) in addition to an independent claim for a given product, and independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for an apparatus or means specially designed for carrying out the said process,...

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

**Group I:** Claims 1-5, 45 and 46 drawn to the compounds and compositions of formula (I).

**Group II:** Claims 6-42 drawn to the method of using the products of formula (I).

**Group III:** Claims 43 and 44 drawn to a diagnostic kit comprising the products of formula (I).

*Advisory of Rejoinder*

The Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejections are governed by 37 CFR 1.116; amendments submitted after allowances are governed by 37 CFR 1.312.

The following is a recitation of M.P.E.P. 821.04, Rejoinder:

Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02(c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims, which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Where the application as originally filed discloses the product and the process for making and/or using the product, and only claims directed to the product are presented for examination, when a

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product claim is found allowable, applicant may present claims directed to the process of making and/or using the patentable product by way of amendment pursuant to 37 CFR 1.121. In view of the rejoinder procedure, and in order to expedite prosecution, applicants are encouraged to present such process claims, preferably as dependent claims, in the application at an early stage of prosecution. Process claims, which depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance. Amendments submitted after final rejection are governed by 37 CFR 1.116. Process claims which do not depend from or otherwise include the limitations of the patentable product will be withdrawn from consideration, via an election by original presentation (see MPEP § 821.03). Amendments submitted after allowance are governed by 37 CFR 1.312. Process claims which depend from or otherwise include all the limitations of an allowed product claim and which meet the requirements of 35 U.S.C. 101, 102, 103, and 112 may be entered.

Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either: (A) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2); or (B) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2) even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26(a) states that "[T]he Commissioner may refund any fee paid by mistake or in excess of that required. A change of purpose after the payment of a fee...will not entitle a party to a refund of such fee..." In this case, the fees paid under 37 CFR 1.129(b) were not paid by mistake nor paid in excess, therefore, applicant would not be entitled to a refund. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action. Form paragraphs 8.42 through 8.44 should be used to notify applicant of the rejoinder of process claims which depend from or otherwise include all the limitations of an allowable product claim.

In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

"However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations** of an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

Pursuant to M.P.E.P. § 821.04 and In re Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is<sup>3</sup> advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Applicant is reminded that upon cancellation of claims to a nonelected invention, the inventions must be amended in compliance with 37 C.F.R. 1.48(b) if one of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. 1.48(b) and by the fee required under 37 C.F.R. 1.17(i). In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

The claims herein lack unity of invention under PCT Rules 13.1 and 13.2 because, pursuant to 37 C.F.R. 1.475(a) the instant invention lacks unity of invention since under 37 CFR 1.475:

Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical feature among those inventions involving one or more of the same or corresponding special technical features...those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

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The structural moiety common to **Groups I-III** is the 1H-indole-2-carboxylic acid moiety, and is therefore the *technical feature*. However, this technical feature is not a *special technical feature*, because it fails to define a contribution over the prior art (*See, Kim et al.*, US 4,350,633, for example). Therefore, Claims 1-46 are not so linked as to form a single general inventive concept and there is a lack of unity of invention. The variables vary extensively and when taken as a whole result in vastly different compounds. Additionally, the vastness of the claimed subject matter and the complications in understanding the claimed subject matter impose a serious burden on any examination of the claimed subject matter.

Because the claims do not relate to a single general inventive concept under PCT Rule 13.1 and lack the same or corresponding special technical features, the claims lack unity of invention and should be limited to a product, a process for the manufacture of said product, or a method of use.

Furthermore, with respect to **Groups I-III**, even if unity of invention under 37 CFR 1.475(a) is not lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specially designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specially designed for carrying out the said process.

Moreover, according to 37 CFR 1.475(c),

If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

In the instant case the claims are drawn to more than one product, process, and method of use. According to 37 CFR 1.475(e),

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even if the restriction requirement is traversed (37 CFR 1.143).

#### **Telephonic Inquiry**

During a telephone conversation with Suet M. Chong, Esquire on or about May 31, 2006 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-5, 45 and 46, directed to a product. Claims 6-44 are hereby withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Applicant is reminded that he/she is required to affirm this election when responding to this Office Action.

#### **V. EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.



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Authorization for this examiner's amendment was given in a telephone interview with Suet Chong, Esquire on June 15, 2006 and June 19, 2006.

The application has been amended as follows:

1. CANCEL CLAIMS: 6 through 44.
2. Claim 1: DELETE "equivalent" on p. 112, line 3.
3. Claim 1: INSERT ---salts, hydrates or optical isomers--- on p. 112, line 3.
4. Claim 4: INSERT ---and--- after 1-3(3-carboxyphenyl)-3-(2-mercaptoethyl)-1H-indole-2-carboxylic acid; --- on p. 114, line 22.
5. Claim 4: DELETE "; and pharmaceutically acceptable equivalents" on p. 114, lines 24-25.
6. Claim 46: INSERT ---and--- after 1-3(3-carboxyphenyl)-3-(2-mercaptoethyl)-1H-indole-2-carboxylic acid; --- on p. 134, line 12.
7. Claim 46: DELETE "; and pharmaceutically acceptable equivalents" on p. 134, lines 14-15.
8. ADD the following Claims:
  47. The pharmaceutical composition of claim 45, wherein:  
A<sup>1</sup>, A<sup>2</sup>, A<sup>3</sup> and A<sup>4</sup> are independently hydrogen or -COOH;  
R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are each hydrogen; and  
R<sup>5</sup> is hydrogen, phenyl, benzyl or phenylethyl, wherein said phenyl, benzyl or phenylethyl are independently substituted with one or more substituent(s).
  48. The pharmaceutical composition of claim 47, wherein R<sup>5</sup> is benzyl substituted with one or more substituent(s) independently selected from the group consisting of carboxy, halo, C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>4</sub> alkoxy.
  49. The pharmaceutical composition of claim 45, wherein the compound is an enantiomer or an enantiomer-enriched mixture.

**V. REASONS FOR ALLOWANCE**

The following is an examiner's statement of reasons for allowance: The instant invention is drawn to a substituted 1H-indole-2 carboxylic acid compound. The instant invention appears to be free of the art of record. The closest prior art reference of record is *Maetzel et al.*, US Patent 4,965,369. The instant invention is free of the art of record because the art of record, also drawn to a 1H-indole-2-carboxylic acid, is not substituted at the 3 position with an alkylmercapto group.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

**VI. CONCLUSION**

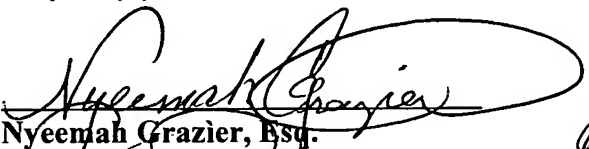
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nyeemah Grazier whose telephone number is (571) 272-8781. The examiner can normally be reached on Monday through Thursday and every other Friday from 8:30 a.m. - 6:00 p.m.

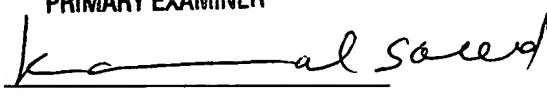
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (571) 272 - 0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Very truly yours,

  
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